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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,060	03/15/2005	Wilhelm Scherze	23240	9011
535 7590 01/10/2008 K.F. ROSS P.C. 5683 RIVERDALE AVENUE SUITE 203 BOX 900 BRONX, NY 10471-0900			EXAMINER WOOD, AMANDA P	
			ART UNIT 1657	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/528,060	<b>Applicant(s)</b> SCHERZE ET AL.	
	<b>Examiner</b> Amanda P. Wood	<b>Art Unit</b> 1657	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 September 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's response and amendments filed on 24 September 2007 have been received and entered.

Claims 1-16 are pending and have been examined on the merits.

Applicant's arguments with respect to the 112, 2<sup>nd</sup> paragraph and 103 rejections of claims 1-14 have been considered but are moot in view of the new ground(s) of rejection.

### ***Withdrawn Rejections***

Based upon the newly submitted amendments to the claims, the 112, 2<sup>nd</sup> paragraph rejections and the 102 rejection of record have been withdrawn.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, step (f) of claim 1 recites that phrase "permanently measuring all cell culture parameters relevant to treating inflammation, cancer, cardiovascular disease, AIDS, relevant to programmed cell death, or relevant to blood coagulation" in lines 1-4 of the step. It is unclear particular parameters Applicant intends to encompass by "all parameters" which would be relevant to each of these conditions and/or diseases, but Applicant only provides the examples of pH

Art Unit: 1657,

values, lactate values, and electric potential. It is unclear from the instant specification what particular parameters, other than the three examples listed by Applicant, would be relevant to the particular diseases and conditions claimed by Applicant. It would appear to the Examiner that different parameters would be relevant for different conditions, and therefore, different sensors would be necessary for each of the different parameters that would be necessary to measure. Therefore, Applicant has failed to particularly point out what types of sensors should be provided in the instant invention, based upon the language of claim 1, step f, as currently drafted.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kearney in view of Vellinger et al (US 7,198,940 B2) and Pfaller (US 6,329,195).

Kearney teaches a method for culturing and testing of cells and tissues in a fully controlled thermal and gaseous environment, using an automated system (i.e., cell culture system) which provides a precision metering system for the introduction of

controlled volumes of media as well as in-line detectors and monitoring devices allowing continuous assessment of the viability and metabolic state of each cell without the need for invasive procedures. Furthermore, Kearney teaches that the system includes a computer control allowing adjustment of rates of oxygenation, nutrient feed, and operation of heat control. Kearney also teaches that the system has a temperature sensor within each bioreactor (i.e., cell culture chamber) in the system which senses the temperature and conveys this information to the onboard computer control to provide accurate temperature control. In addition, Kearney teaches that appropriate sensors are provided within the gas pathway to sense dissolved oxygen and/or acidity (see, for example, col. 6, lines 10-25). Kearney further teaches that a computer-controlled fluid pathway provides a supply of media, nutrients and chemical agents to the cells of the bioreactors, allowing control of administration of fluids as well as removal thereof. The bioreactors can be connected either in series or in parallel, according to Kearney (see, for example, col. 5, lines 55-67, col. 6, lines 1-10, col. 20, lines 30-50). Furthermore, Kearney teach that gases are continuously passed from bioreactor to bioreactor via a series of serially disposed T-unions (see, for example, col. 14, lines 45-67). In addition, Kearney teaches that the invention can include an automated microscope/CCD camera system to allow direct microscopic analysis of living cells during the study (see, for example, col. 20, lines 15-35). Kearney further teaches that determining the biotransformation of test materials can be accomplished by connecting two bioreactors in series, wherein the first bioreactor contains a target tissue and the second bioreactor contains hepatic tissue, and effluent from the second bioreactor may be removed for

Art Unit: 1657

analytical testing, or cells may be observed directly (see, for example, col. 20, lines 30-67).

Kearney does not expressly teach a method wherein the cell culture is permanently microscopically observed.

Vellinger et al beneficially teach a bioreactor apparatus and cell culturing system wherein an electronic video microscope provides real-time and recorded and/or transmitted observation of cells in the culture (see, for example, Abstract). Furthermore, Vellinger et al teach that the video concept provides the capability to observe the bioreactor as well as microscopic observation of individual cells. Vellinger et al teach that the observation system comprises a camera and a dual optical path configuration allowing for an observation of the cell growth reactor vessel contents and a second microscopic observation path for observation of the cell sample (see, for example, claim 17). In addition, Vellinger et al beneficially teach that the image capture is controlled by a programmed routine (see, for example, col. 8, lines 10-67). Additionally, Vellinger et al beneficially teach that the cell culture system provided has physiological sensors for pH, glucose and oxygen (see, for example, col. 4, lines 30-50).

Kearney and Vellinger et al do not expressly teach a method wherein one cell culture, each of a different type, is established on both sides of a gas-permeable membrane inside at least one cell culture chamber for the purpose of a direct co-cultivation of both cell cultures.

Pfaller beneficially teaches a cell culture support and method for co-culturing cells wherein the inflow and outflow channels are designed to provide homogenous

replacement of medium, thereby offering the possibility to perfuse nutrients of different composition at the top (apical) and bottom (basal or basolateral) side of the cell culture growth support. Pfaller further beneficially teaches that the cell culture growth support is bounded by a gas permeable membrane on both sides, and therefore, Pfaller teaches a method wherein different cell types are cultured on both sides of a gas permeable membrane in a cell culture chamber for direct co-cultivation.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method and system of culturing cells disclosed by Kearney based upon the beneficial teachings provided by Vellinger et al, with respect to providing a camera and microscope for observation of a cell culture chamber, and by Pfaller, with respect to the art-recognized method of co-culturing cells by providing two different nutrient compositions to apical and basolateral cells, as discussed above. Kearney specifically teaches that his automated cell culturing system can be used for co-culturing cells, and that co-cultures of rat myocytes and neuronal tissue have been grown and tested using the system. Vellinger et al particularly teach that a camera and microscope system which provides real-time images of a cell culture chamber wherein the images captured by the camera are controlled by a programmed routine, is a known method for observing cell cultures in bioreactors. Additionally, Vellinger et al, in addition to Kearney, teach that sensors for pH and oxygen are provided in the cell culture chambers known in the art, and that the cell culture chambers can be used to test and culture cells and tissues, and therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was

made to measure cell culture parameters relevant to such cultures for the purpose of conducting the tests. Pfaller specifically teaches a method and apparatus that has an advantage over other cell culture systems in that it provides means for continuous replacement of culture medium while allowing for defined partial pressures of gases in immediate contact with the culture medium due to the use of a membrane impermeable to liquids but permeable to gases. Furthermore, Pfaller teaches that such a system allows for the perfusion of different medium to the apical and basolateral sides of the cell culture support, thereby providing organotypic culture conditions. Therefore, it would have been both obvious and beneficial for one of ordinary skill in the art to modify the methods and systems provided by Kearney using the methods of Pfaller, so as to provide a method for direct co-culture of cells while still providing a self-contained environment free from contamination, for the expected benefit of culturing cells under conditions similar to that found in vivo.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.



***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No Claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1657

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW  
Examiner  
Art Unit 1657

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CHRISTOPHER R. TATE  
PRIMARY EXAMINER